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- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
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- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



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(54) Title: ABC1 MODULATION FOR THE MODULATION OF CHOLESTEROL TRANSPORT

(57) Abstract: Methods and compounds are disclosed for lowering serum LDL levels or serum cholesterol levels, or for reducing the transport of cholesterol from the gut to the blood or the lymph, based on the observation that a gene known as ABC1 is necessary in order for cholesterol to be transported from the intestinal lumen into the bloodstream. A mutant chicken phenotype, known as the WHAM chicken, characterized by low levels of serum LDL and reduced transport of cholesterol, facilitated the discovery of this function of the ABC1 gene. Techniques which act to inhibit ABC1 activity in the cells of the intestinal wall will result in lower serum cholesterol.

INTERNATIONAL SEARCH REPORT

national Application No
PCT/US 00/30109

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/64 A61P3/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 00 34461 A (MANGELSDORF DAVID J ;DIETSCHY JOHN M (US); REPA JOYCE J (US); UNIV) 15 June 2000 (2000-06-15) abstract page 14, line 10 - line 30 page 15, line 24 - line 31 ---	1-6, 11
X	WO 98 57649 A (SMITH STEPHEN ALISTAIR ;SMITHKLINE BEECHAM PLC (GB)) 23 December 1998 (1998-12-23) page 2, line 32 -page 3, line 3 page 6, line 4-7 --- -/-	1-6, 11

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

B document member of the same patent family

Date of the actual completion of the international search

28 June 2001

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26.07.01

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INTERNATIONAL SEARCH REPORT

national Application No
PCT/US 00/30109

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SCHMITZ G ET AL: "ATP-BINDING CASSETTE TRANSPORTER A1 (ABCA1) IN MACROPHAGES: A DUAL FUNCTION IN INFLAMMATION AND LIPID METABOLISM?" PATHOBIOLOGY, KARGER, BASEL, CH, vol. 67, no. 5/06, 1999, pages 236-240, XP000971329 ISSN: 1015-2008 page 237, right-hand column, line 1 - line 15 page 238, right-hand column, line 1 - line 16 figure 2	1-6, 11
Y	HAMON YANNICK ET AL: "Interleukin-1-beta secretion is impaired by inhibitors of the Atp binding cassette transporter, ABC1." BLOOD, vol. 90, no. 8, 1997, pages 2911-2915, XP002150651 ISSN: 0006-4971 abstract page 2911, right-hand column, line 5 - line 7	1-6, 11
Y	OWEN JAMES S: "Role of ABC1 gene in cholesterol efflux and atheroprotection." LANCET (NORTH AMERICAN EDITION), vol. 354, no. 9188, 23 October 1999 (1999-10-23), pages 1402-1403, XP000984726 ISSN: 0099-5355 page 1402, right-hand column, line 37 - line 57	1-6, 11
P, X	WO 00 55318 A (UNIV BRITISH COLUMBIA ; XENON BIORESEARCH INC (CA)) 21 September 2000 (2000-09-21) abstract page 7, line 16 - line 31 page 39, line 19 - page 40, line 1 page 59, line 10 - line 28 page 61, line 22 - line 28	8-10, 12-16
P, X	WO 00 18912 A (BAYER AG ; KLUCKEN JOCHEN (DE); SCHMITZ GERD (DE)) 6 April 2000 (2000-04-06) abstract page 5, line 7 - line 12	8-10, 12-16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/30109

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 17-21
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 17-21

Present claims 17-21 relate to a compound defined by reference to a desirable characteristic or property, namely the ability to be identified as a drug for the reduction of cholesterol transport from the gut to the blood or lymph through a screening for its ability to modulate ABC1 activity.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for glyburide only. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has not been carried out for said claims. The use of glyburide for the preparation of medicaments for the reduction of cholesterol uptake from the gut has been searched in the context of invention 1 (claims 1-6,11, see non unity section).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-6,11

Use of ABC1 inhibitors, in particular sulfonylureas, for inhibiting cholesterol uptake in the gut

2. Claim : 7

Method for testing humans for ABC1 gene allele

3. Claims: 8-10,12-16

Methods for identifying ABC1 inhibitors, testing them and screening for their ability to reduce cholesterol uptake from the gut.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/30109

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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WO 9857649	A	23-12-1998	AU	8539298 A	04-01-1999
			BG	104058 A	31-10-2000
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